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CASE REPORT

Bilateral adrenal hemorrhage in polycythemia vera

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Bilateral adrenal hemorrhage (BAH) is a rare complication typically seen in critically ill patients, which can lead to acute adrenal insufficiency and death unless it is recognized promptly and treated appropriately. We describe the case of a 64-year-old man with polycythemia vera found to be unresponsive with fever, hypotension, tachycardia, and hypoglycemia. Electrocardiogram showed ST-elevation with elevated troponin, hemoglobin, prothrombin time, and partial thromboplastin time. He required aggressive ventilator and vasopressor support. Despite primary coronary intervention, he remained hypotensive. Random cortisol level was low. He received stress dose hydrocortisone with immediate hemodynamic stability. BAH was highly suspected and was confirmed by non-contrast abdominal computed tomography. Prompt recognition and timely initiated treatment remain crucial to impact the mortality associated with acute adrenal insufficiency.

Keywords: *polycythemia vera*; *bilateral adrenal hemorrhage*; *adrenal insufficiency*

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Bilateral adrenal hemorrhage (BAH) is a rare complication typically seen in critically ill patients, which can lead to acute adrenal insufficiency and death unless it is recognized promptly and treated appropriately (1–3).

Case description

A 64-year-old man with polycythemia vera (PV) was brought to the emergency department after being found unresponsive in his apartment. He was noted to be hypotensive (72/43 mmHg), tachycardic (115 beats/min), febrile (38.8°C), and hypoglycemic (38 mg/dL). History revealed that the patient had headache and profuse vomiting for a few days before admission. He was a current active smoker and remote heavy alcohol user. On physical examination, he was unresponsive but otherwise unremarkable except for a tense abdomen and poorly perfused distal lower extremities (no palpable pulses). Dry gangrenous and ischemic changes were noted in his left toes. Electrocardiogram demonstrated an acute inferolateral ST-elevation.

On initial laboratory results (Table 1), several abnormalities were seen including leukocytosis, acute kidney injury with hyperkalemia, hyperbilirubinemia, elevated troponin, and elevated coagulation parameters with a normal platelet count.

Initial diagnosis was thought to be cardiogenic shock from myocardial infarction. The patient required mechanical ventilation, aggressive hemodynamic support, and glucose replacement. Broad-spectrum antibiotics were initiated given the possibility of sepsis. Cardiac catheterization showed occlusive thrombus within the left anterior descending artery, and a bare-metal stent was placed. There was no coronary evidence of atherosclerosis. Despite primary coronary intervention, he remained hypotensive and critically ill. His random cortisol level was 3.3 mcg/dL (7.0–25.0 mcgs/dL). Stress dose (100 mg) hydrocortisone resulted in immediate restoration of hemodynamics. Due to rapid response to glucocorticoid, in the setting of underlying PV, BAH was suspected. Non-contrast abdominal computed tomography (CT) scan confirmed BAH (Fig. 1).

He had a prompt clinical and laboratory improvement. Antibiotics were stopped. Hydrocortisone therapy was eventually weaned to replacement dose for treatment of chronic primary adrenal insufficiency.

Discussion

Our patient in the setting of underlying PV presented with clinical features of coagulopathy including myocardial infarction, peripheral gangrene, and elevated international normalized ratio (INR). Classic findings of adrenal insufficiency were seen and included: circulatory shock, hypoglycemia, hyperkalemia, azotemia (4–6), and unexplained transaminitis (7–10).

PV is a myeloproliferative disorder characterized by clonal proliferation of hematopoietic stem cells leading to an accumulation of erythrocytes, leukocytes, and platelets within the circulation. Thrombotic and hemorrhagic

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Table 1. Laboratory testing results at admission

Test	Result	Reference range
Comprehensive metabolic panel		
Sodium	135	135–145 mmol/L
Potassium	5.4	3.5–5.1 mmol/L
Chloride	98	98–107 mmol/L
Bicarbonate	25	21–32 mmol/L
Blood urea nitrogen	71	7.0–20.0 mg/dL
Creatinine	2.43	0.5–1.3 mg/dL
Glucose	178	70–99 mg/dL
Alanine aminotransferase	49	12–78 unit/L
Aspartate aminotransferase	122	3–37 unit/L
Alkaline phosphatase	145	12–78 unit/L
Total protein	5.8	6.4–8.2 g/dL
Total bilirubin	4.7	0.2–1 mg/dL
Complete blood count		
White blood cells	12.35	4.7–11.0 k/mm^3
Hemoglobin	20.5	13.2–18.0 g/dL
Hematocrit	62.5	39–49%
Platelet	338	189–440 k/mm^3
Cardiac markers		
Troponin I	34.5	$<$0.04–0.09 ng/ml
Myoglobin	649	14.0–106.0 ng/ml
Coagulation studies		
PT/INR (Prothrombin time)	73.9/7.2	9.7–11.9 sec (0.9–1.1)
APTT (Partial thromboplastin time)	49	23.1–34.1 sec

complications are major causes of morbidity and mortality in PV. Little is known about the mechanisms of thrombogenesis in patients with PV but clinical data have related it to elevated platelet count, increased hematocrit and red blood cell adhesiveness, leukocytosis, inflammation, and

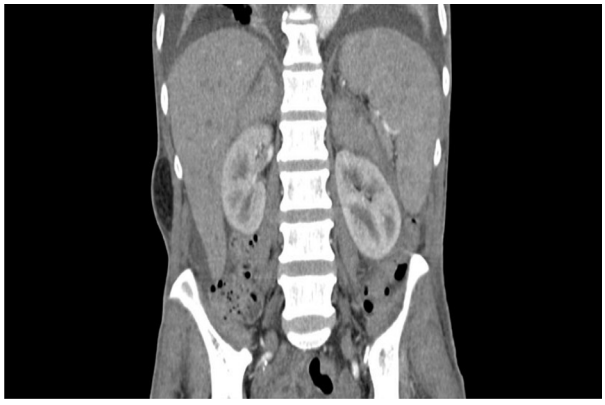

Fig. 1. Computed tomography of abdomen demonstrating bilateral adrenal hemorrhage with right adrenal gland measuring 5.3 cm superior to inferior $\times$3.4 cm transversely $\times$3.8 cm anterior to posterior, and the left adrenal gland measuring 6.1 cm superior to inferior $\times$4.3 cm transversely $\times$5.4 cm anterior to posterior.

Table 2. Causes of adrenal hemorrhage

Trauma

Stress
- Surgery
- Sepsis
- Burns
- Hypotension
- Pregnancy
- Exogenous adrenocorticotropic hormone
- Exogenous steroids

Hemorrhagic diathesis and coagulopathy
- Anticoagulants
- Antiphospholipid antibodies
- Disseminated intravascular coagulopathy

Underlying adrenal tumors
- Myelolipoma
- Pseudocyst
- Hemangioma
- Pheochromocytoma
- Adrenocortical tumor
- Adenoma
- Metastases

Neonatal stress

elevated *JAK2*^{V617F} allele (11, 12). Coronary events are common in patients with PV accounting for 45% of all-cause mortality. Myocardial infarction was seen in 0.9% of the patients and was due to arterial thrombosis (13).

Although it is well-known that thrombosis and hemorrhage are common features of PV, to our knowledge, there were only two reported cases connecting PV and hemorrhage within the adrenal glands (14, 15). Gelfand (14) reported occurrence of BAH in an 85-year-old man with PV associated with thrombocytosis who presented with syncope and abdominal tenderness. Gelfand, thus, concluded that coagulopathy is what appears to link PV with BAH. Gonen et al. (15) described another case of BAH in a 56-year-old man with PV who presented with epigastric discomfort, nausea, and vomiting. BAH was attributed to high thrombocyte count.

Adrenal hemorrhage has a prevalence of about 1.1% based on autopsy studies (16). With the advent of imaging technology, adrenal hemorrhage is being diagnosed with increasing frequency. Different causes of adrenal hemorrhage are described in Table 2 (17). The pathophysiology of BAH is still unknown. However, due to particular anatomy of its vascular supply adrenal gland is at risk of venous congestion and thrombosis. About 50 to 60 small branches from the 3 suprarenal arteries feed into a subcapsular plexus that drains into the medullary sinusoids by few small venules forming a large central vein. The transition from artery to capillary plexus is abrupt and constitutes a 'vascular dam'. This complex microvascular system of the adrenal glands predispose them to be

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vulnerable to thrombosis or hemorrhagic necrosis in the setting of bleeding associated with severe stress, sepsis, shock, and/or anticoagulation of prolonged duration or to microvascular ischemia and subsequent hemorrhagic infarction in thrombotic conditions (2–4, 18, 19).

Hormonal evidence of adrenal insufficiency and anatomic proof of hemorrhage must be available to confirm diagnosis of BAH (2, 4, 18). Basal cortisol and Adrenocorticotropic hormone (ACTH) levels, and a cosyntropin stimulation test can be used to establish the diagnosis of adrenal insufficiency (20). In patients suspected of adrenal insufficiency, the recommended confirmatory test is the corticotropin stimulation test with intravenous administration of 250 μg of cosyntropin, followed by measuring the serum cortisol value 30 or 60 min later. Peak cortisol <18 mcg/dl indicates adrenal insufficiency. If corticotropin stimulation test is not feasible, a morning cortisol <5 mcg/dl in combination with ACTH can be used.

Various imaging modalities can be used to diagnose adrenal hemorrhage – ultrasonography, CT, and magnetic resonance imaging. Ultrasonography is the preferred imaging modality to diagnose adrenal hemorrhage in neonates. Abdominal CT scan is the most reliable and a widely available method for demonstrating the anatomical evidence of adrenal hemorrhage (3). Acute to subacute hematomas will have high attenuation, ranging from 50 to 90 Hounsfield units. CT is most useful and easily performed in critically ill patients. MRI can be used to gauge the age of the adrenal hematoma and determine if there is any other solid component in the hematoma that might represent an underlying adrenal tumor (21).

BAH may result in complete and irreversible loss of adrenal function, shock, and death, if treatment is delayed or if left untreated. Due to consequent gland atrophy, chronic steroid therapy is required as a life-sustaining treatment.

Conclusion

This case illustrates the importance of being aware of the risk factors for BAH in critically ill patients. The presence of hypercoagulability and refractory hypotension should raise clinical suspicion of BAH. Abdominal CT scan, while valuable in establishing diagnosis of adrenal hemorrhage, must not delay initiation of lifesaving corticosteroid therapy.

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